

04/01

Docket No. A061CIP2

#5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Gregory R. Mundy and Toshiyuki Yoneda  
Application No.: 10/086,217  
Confirmation No.: 5114  
Filed : February 21, 2002  
For : METHODS OF TREATING MULTIPLE MYELOMA AND  
MYELOMA-INDUCED BONE RESORPTION USING  
INTEGRIN ANTAGONISTS  
Group Art Unit : 1644  
Examiner : Not yet assigned

New York, New York  
June 21, 2002

Hon. Commissioner  
for Patents  
Washington, D.C. 20231

TRANSMITTAL LETTER FOR  
INFORMATION DISCLOSURE STATEMENT

Sir:

Transmitted herewith is an Information Disclosure  
Statement in the above-identified application. This  
Statement is submitted:

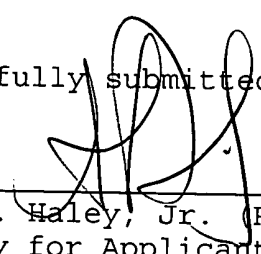
- ☐ [ ] within three months of the application filing date;
- ☒ [X] more than three months from the application filing date but before the mailing date of the first Office Action on the merits.

In accordance with 37 C.F.R. § 1.97, submission of  
this Statement requires no fee. However, if for any reason  
a fee is due, the Director is hereby authorized to charge

EI187452145US

payment of any fees required in connection with this  
Information Disclosure Statement to Deposit Account  
No. 06-1075. A duplicate copy of this letter is transmitted  
herewith.

Respectfully submitted,



---

James F. Haley, Jr. (Reg. No. 27,794)  
Attorney for Applicants  
Stanley D. Liang (Reg. No. 43,753)  
Agent for Applicants  
c/o FISH & NEAVE  
Customer No. 1473  
1251 Avenue of the Americas  
New York, New York 10020-1104  
Tel.: (212) 596-9000



A061CIP2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Gregory R. Mundy and Toshiyuki Yoneda  
Application No. : 10/086,217  
Confirmation No. : 5114  
Examiner : Not yet assigned  
Group Art Unit : 1644  
Filed : February 21, 2002  
For : METHODS OF TREATING MULTIPLE MYELOMA AND  
MYELOMA-INDUCED BONE RESORPTION USING  
INTEGRIN ANTAGONISTS

New York, New York  
June 21, 2002

Hon. Commissioner for Patents  
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. § 1.97 AND 1.56

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants make of record the following  
document in the above-identified patent application, copies of which are submitted herewith:

United States Patent Application Publications

Mundy et al.	US 2002/0022028 A1	published February 21, 2002
Mundy et al.	US 2002/0041874 A1	published April 11, 2002

EI187452145US

### Other References

Alsina, M. et al., "Development of an In Vivo Model of Human Multiple Myeloma Bone Disease," BLOOD 87: 1495-1501 (1996).

Attal, M. et al., "A Prospective, Randomized Trial of Autologous Bone Marrow Transplantation and Chemotherapy in Multiple Myeloma," N ENGL J MED 335: 91-97 (1996).

Atkins, C., "Correspondence: High-Dose Chemotherapy in Multiple Myeloma," N ENGL J MED 335: 1844 (1996).

Oivanen, T. M. et al., "Correspondence: High-Dose Chemotherapy in Multiple Myeloma," N ENGL J MED 335: 1844-1845 (1996).

Attal, M. et al., "Correspondence: High-Dose Chemotherapy in Multiple Myeloma - In Reply," N ENGL J MED 335: 1844-1845 (1996).

Barlogie, B. et al., "Extended survival in advanced and refractory multiple myeloma after single-agent thalidomide: identification of prognostic factors in a phase 2 study of 169 patients," BLOOD 98: 492-494 (2001).

Bataille, R. et al., "Serum Levels of Interleukin 6, a Potent Myeloma Cell Growth Factor, as a Reflect of Disease Severity in Plasma Cell Dyscrasias," J CLIN INVEST 84: 2008-2011 (1989).

Bataille, R. et al., "Mechanisms of Bone Lesions In Multiple Myeloma," HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA 6: 285-295 (1992).

Bataille, R. et al., "Biologic Effects of Anti-Interleukin-6 Murine Monoclonal Antibody in Advanced Multiple Myeloma," BLOOD 86: 685-691 (1995).

- Berenson, J. R. et al., "Long-Term Pamidronate Treatment of Advanced Multiple Myeloma Patients Reduces Skeletal Events," J CLIN ONCOL 16: 593-602 (1998).
- Seymour, J. F., "Correspondence: Long-Term Pamidronate in Multiple Myeloma," J CLIN ONCOL 16: 2572 (1998).
- Berenson, J. R., "Correspondence: Long-Term Pamidronate in Multiple Myeloma - In Reply," J CLIN ONCOL 16: 2572-2573 (1998).
- Boyce, B. F. et al., "Bolus Injections of Recombinant Human Interleukin-1 Cause Transient Hypocalcemia in Normal Mice," ENDOCRINOLOGY 125: 2780-2783 (1989).
- Chauhan, D. et al., "Regulation of Interleukin 6 in Multiple Myeloma and Bone Marrow Stromal Cells," STEM CELLS 13 (suppl 2): 35-39 (1995).
- Dallas, S. L. et al., "Ibandronate Reduces Osteolytic Lesions but not Tumor Burden in a Murine Model of Myeloma Bone Disease," BLOOD 93: 1697-1706 (1999).
- Epstein, J., "Myeloma Phenotype: Clues To Disease Origin and Manifestation," HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA 6:249-256 (1992).
- Garrett, I. R. et al., "A Murine Model of Human Myeloma Bone Disease," BONE 20: 515-520 (1997).
- Gossler, U. et al., "Predominant Role of  $\alpha 4$ -integrins for distinct steps of lymphoma metastasis," Proc. Natl. Acad. Sci. USA 93: 4821-4826 (1996).
- MacDonald, B. R. et al., "Effects of Human Recombinant CSF-GM and Highly Purified CSF-1 on the Formation of Multinucleated Cells with Osteoclast Characteristics in Long-Term Bone Marrow Cultures," J BONE AND MINERAL RESEARCH 1: 227-233 (1986).

Matsuura, N. et al., "Induction of Experimental Bone Metastasis in Mice by Transfection of Integrin  $\alpha 4 \beta 1$  into Tumor Cells," AM J PATHOL 148: 55-61 (1996).

Michigami, T. et al., "Interactions of Myeloma Cells with Bone Marrow Stromal Cells Via  $\alpha 4 \beta 1$  Integrin-VCAM-1 Is Required For the Development of Osteolysis," Nineteenth Annual Meeting of the American Society for Bone and Mineral Research, Cincinnati, Ohio: Abstract 104 (9/14/1997); J. BONE AND MINERAL RESEARCH 12 Supplement: p. S218 (1997).

Michigami, T. et al., "Cell-cell contact between marrow stromal cells and myeloma cells via VCAM-1 and  $\alpha 4 \beta 1$ -integrin enhances production of osteoclast-stimulating activity," BLOOD 96: 1953-1960 (2000).

Mittelman, M. et al., "Erythropoietin induces tumor regression and antitumor immune responses in murine myeloma models," Proc. Natl. Acad. Sci. USA 98: 5181-5186 (2001).

Mori, Y. et al., "Anti- $\alpha 4$  Integrin Antibody Suppresses the Bone Disease of Myeloma and Disrupts Myeloma-Marrow Stromal Cell Interactions," Twenty-First Annual Meeting of the American Society for Bone and Mineral Research, St. Louis, Missouri: Abstract 1161 (10/3/1999); J. BONE AND MINERAL RESERACH 14 Supplement 1: p. S148 (1999).

Mundy, G. R. and Bertolini, D. R., "Bone Destruction and Hypercalcemia in Plasma Cell Myeloma," SEMINARS IN ONCOLOGY 13: 291-299 (1986).

Mundy, G. R., "Myeloma Bone Disease," EURO J CANCER 34: 246-251 (1998).

Oyajobi, B. O. et al., "Expression of Rank Ligand (RankL) By Myeloma Cells Requires Binding To Bone Marrow Stromal Cells Via An  $\alpha 4 \beta 1$ -VCAM-1 Interaction," Second

Joint Meeting of The American Society for Bone and Mineral Research and The International Bone and Mineral Society, San Francisco, California: Abstract 1133 (12/4/1998); BONE 23(5 Supplement): p. S180 (1998).

Papayannopoulou, T. and Nakamoto, B., "Peripheralization of hemopoietic progenitors in primates treated with anti-VLA<sub>4</sub> integrin," Proc. Natl. Acad. Sci. USA 90: 9374-9378 (1993).

Qian, F. et al., "Expression of the Integrin  $\alpha 4 \beta 1$  on Melanoma Cells Can Inhibit the Invasive Stage of Metastasis Formation," CELL 77: 335-347 (1994).

Shimizu, N. et al., "Disruption of Cell-Cell Contact with Stromal Cells Using Anti- $\alpha 4$  integrin Antibody Enhances Sensitivity of Myeloma Cells to Melphalan in Vitro and in Vivo," Twenty-Third Annual Meeting of the American Society for Bone and Mineral Research, Phoenix, Arizona: Presentation Number SU078 (10/14/2001).

Tinhofer, I. et al., "Expression of functional interleukin-15 receptor and autocrine production of interleukin-15 as mechanisms of tumor propagation in multiple myeloma," BLOOD 95: 610-618 (2000).

Vanderkerken, K. et al., "Organ involvement and phenotypic adhesion profile of 5T2 and 5T33 myeloma cells in the C57BL/KaLwRij mouse," BRIT J CANCER 76: 451-460 (1997).

Applicants request that these documents be (1) fully considered by the Examiner during the examination of this application; and (2) printed on any patent that may issue from this application.

Applicants also request that a copy of Form PTO-1449, as considered and initialed by the Examiner, be returned with the next communication.



---

James F. Haley, Jr. (Reg. No. 27,794)  
Attorney for Applicants  
Stanley D. Liang (Reg. No. 43,753)  
Agent for Applicants  
c/o FISH & NEAVE (Customer No. 1473)  
1251 Avenue of the Americas  
New York, New York 10020-1104  
Tel.: (212) 596-9000  
Fax.: (212) 596-9090



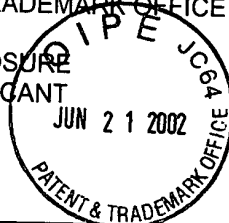
DEPT. OF COMMERCE  
PATENT & TRADEMARK OFFICE

RECEIVED  
JUN 21 2002

DEPT. OF COMMERCE  
PATENT & TRADEMARK OFFICE

EI187452145US

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEINFORMATION DISCLOSURE  
STATEMENT BY APPLICANTATTY. DOCKET NO.  
A061CIP2SERIAL NO.  
10/086,217APPLICANT  
Gregory R. Mundy and  
Toshiyuki YonedaCONFIRMATION NO.  
5114FILING DATE  
February 21, 2002GROUP  
1644

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	Alsina, M. et al., "Development of an In Vivo Model of Human Multiple Myeloma Bone Disease," <u>BLOOD</u> 87: 1495-1501 (1996).
	Attal, M. et al., "A Prospective, Randomized Trial of Autologous Bone Marrow Transplantation and Chemotherapy in Multiple Myeloma," <u>N ENGL J MED</u> 335: 91-97 (1996).
	Atkins, C., "Correspondence: High-Dose Chemotherapy in Multiple Myeloma," <u>N ENGL J MED</u> 335: 1844 (1996).
	Oivanen, T. M. et al., "Correspondence: High-Dose Chemotherapy in Multiple Myeloma," <u>N ENGL J MED</u> 335: 1844-1845 (1996).
	Attal, M. et al., "Correspondence: High-Dose Chemotherapy in Multiple Myeloma - In Reply," <u>N ENGL J MED</u> 335: 1844-1845 (1996).
	Barlogie, B. et al., "Extended survival in advanced and refractory multiple myeloma after single-agent thalidomide: identification of prognostic factors in a phase 2 study of 169 patients," <u>BLOOD</u> 98: 492-494 (2001).
	Bataille, R. et al., "Serum Levels of Interleukin 6, a Potent Myeloma Cell Growth Factor, as a Reflect of Disease Severity in Plasma Cell Dyscrasias," <u>J CLIN INVEST</u> 84: 2008-2011 (1989).
	Bataille, R. et al., "Mechanisms of Bone Lesions In Multiple Myeloma," <u>HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA</u> 6: 285-295 (1992).
	Bataille, R. et al., "Biologic Effects of Anti-Interleukin-6 Murine Monoclonal Antibody in Advanced Multiple Myeloma," <u>BLOOD</u> 86: 685-691 (1995).
	Berenson, J. R. et al., "Long-Term Pamidronate Treatment of Advanced Multiple Myeloma Patients Reduces Skeletal Events," <u>J CLIN ONCOL</u> 16: 593-602 (1998).
	Seymour, J. F., "Correspondence: Long-Term Pamidronate in Multiple Myeloma," <u>J CLIN ONCOL</u> 16: 2572 (1998).
	Berenson, J. R., "Correspondence: Long-Term Pamidronate in Multiple Myeloma - In Reply," <u>J CLIN ONCOL</u> 16: 2572-2573 (1998).
	Boyce, B. F. et al., "Bolus Injections of Recombinant Human Interleukin-1 Cause Transient Hypocalcemia in Normal Mice," <u>ENDOCRINOLOGY</u> 125: 2780-2783 (1989).
	Chauhan, D. et al., "Regulation of Interleukin 6 in Multiple Myeloma and Bone Marrow Stromal Cells," <u>STEM CELLS</u> 13 (suppl 2): 35-39 (1995).
	Dallas, S. L. et al., "Ibandronate Reduces Osteolytic Lesions but not Tumor Burden in a Murine Model of Myeloma Bone Disease," <u>BLOOD</u> 93: 1697-1706 (1999).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEINFORMATION DISCLOSURE  
STATEMENT BY APPLICANTATTY. DOCKET NO.  
A061CIP2SERIAL NO.  
10/086,217APPLICANT  
Gregory R. Mundy and  
Toshiyuki YonedaCONFIRMATION NO.  
5114FILING DATE  
February 21, 2002GROUP  
1644

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

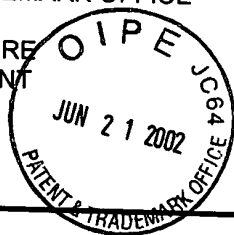
EXAMINER INITIAL	
	Epstein, J., "Myeloma Phenotype: Clues To Disease Origin and Manifestation," <u>HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA</u> 6:249-256 (1992).
	Garrett, I. R. et al., "A Murine Model of Human Myeloma Bone Disease," <u>BONE</u> 20: 515-520 (1997).
	Gosslar, U. et al., "Predominant Role of $\alpha 4$ -integrins for distinct steps of lymphoma metastasis," <u>Proc. Natl. Acad. Sci. USA</u> 93: 4821-4826 (1996).
	MacDonald, B. R. et al., "Effects of Human Recombinant CSF-GM and Highly Purified CSF-1 on the Formation of Multinucleated Cells with Osteoclast Characteristics in Long-Term Bone Marrow Cultures," <u>J BONE AND MINERAL RESEARCH</u> 1: 227-233 (1986).
	Matsuura, N. et al., "Induction of Experimental Bone Metastasis in Mice by Transfection of Integrin $\alpha 4 \beta 1$ into Tumor Cells," <u>AM J PATHOL</u> 148: 55-61 (1996).
	Michigami, T. et al., "Interactions of Myeloma Cells with Bone Marrow Stromal Cells Via $\alpha 4 \beta 1$ Integrin-VCAM-1 Is Required For the Development of Osteolysis," <u>Nineteenth Annual Meeting of the American Society for Bone and Mineral Research, Cincinnati, Ohio</u> : Abstract 104 (9/14/1997); <u>J. BONE AND MINERAL RESEARCH</u> 12 Supplement: p. S218 (1997).
	Michigami, T. et al., "Cell-cell contact between marrow stromal cells and myeloma cells via VCAM-1 and $\alpha 4 \beta 1$ -integrin enhances production of osteoclast-stimulating activity," <u>BLOOD</u> 96: 1953-1960 (2000).
	Mittelman, M. et al., "Erythropoietin induces tumor regression and antitumor immune responses in murine myeloma models," <u>Proc. Natl. Acad. Sci. USA</u> 98: 5181-5186 (2001).
	Mori, Y. et al., "Anti- $\alpha 4$ Integrin Antibody Suppresses the Bone Disease of Myeloma and Disrupts Myeloma-Marrow Stromal Cell Interactions," <u>Twenty-First Annual Meeting of the American Society for Bone and Mineral Research, St. Louis, Missouri</u> : Abstract 1161 (10/3/1999); <u>J. BONE AND MINERAL RESEARCH</u> 14 Supplement 1: p. S148 (1999).
	Mundy, G. R. and Bertolini, D. R., "Bone Destruction and Hypercalcemia in Plasma Cell Myeloma," <u>SEMINARS IN ONCOLOGY</u> 13: 291-299 (1986).
	Mundy, G. R., "Myeloma Bone Disease," <u>EURO J CANCER</u> 34: 246-251 (1998).
	Oyajobi, B. O. et al., "Expression of Rank Ligand (RankL) By Myeloma Cells Requires Binding To Bone Marrow Stromal Cells Via An $\alpha 4 \beta 1$ -VCAM-1 Interaction," <u>Second Joint Meeting of The American Society for Bone and Mineral Research and The International Bone and Mineral Society, San Francisco, California</u> : Abstract 1133 (12/4/1998); <u>BONE</u> 23(5 Supplement): p. S180 (1998).
	Papayannopoulou, T. and Nakamoto, B., "Peripheralization of hemopoietic progenitors in primates treated with anti-VLA <sub>4</sub> integrin," <u>Proc. Natl. Acad. Sci. USA</u> 90: 9374-9378 (1993).
	Qian, F. et al., "Expression of the Integrin $\alpha 4 \beta 1$ on Melanoma Cells Can Inhibit the Invasive Stage of Metastasis Formation," <u>CELL</u> 77: 335-347 (1994).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEINFORMATION DISCLOSURE  
STATEMENT BY APPLICANTATTY. DOCKET NO.  
A061CIP2SERIAL NO.  
10/086,217APPLICANT  
Gregory R. Mundy and  
Toshiyuki YonedaCONFIRMATION NO.  
5114FILING DATE  
February 21, 2002GROUP  
1644

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	Shimizu, N. et al., "Disruption of Cell-Cell Contact with Stromal Cells Using Anti- $\alpha$ 4integrin Antibody Enhances Sensitivity of Myeloma Cells to Melphalan in Vitro and in Vivo," <u>Twenty-Third Annual Meeting of the American Society for Bone and Mineral Research, Phoenix, Arizona</u> : Presentation Number SU078 (10/14/2001).
	Tinhofer, I. et al., "Expression of functional interleukin-15 receptor and autocrine production of interleukin-15 as mechanisms of tumor propagation in multiple myeloma," <u>BLOOD</u> 95: 610-618 (2000).
	Vanderkerken, K. et al., "Organ involvement and phenotypic adhesion profile of 5T2 and 5T33 myeloma cells in the C57BL/KaLwRij mouse," <u>BRIT J CANCER</u> 76: 451-460 (1997).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.